

01997.001700.



PATENT APPLICATION

1645  
S  
B

10/11/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

ANJANA RAO, ET AL.

Application No.: 10/058,024

Filed: January 29, 2002

For: ANERGY-REGULATED  
MOLECULES

Examiner: Not Yet Assigned

Group Art Unit: 1645

July 30, 2002

RECEIVED

AUG 01 2002

TECH CENTER 1600/2900

Commissioner for Patents  
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56 and in accordance with the practice under 37 C.F.R. §§ 1.97 and 1.98, the Examiner's attention is directed to the documents listed on the enclosed Form PTO-1449. Copies of the listed documents are also enclosed.

It is respectfully requested that the above information be considered by the Examiner and that a copy of the enclosed Form PTO-1449 be returned indicating that such information has been considered.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address given below.

RECEIVED

Respectfully submitted,

AUG 01 2002

Royal R Mandel TECH CENTER 1600/2900  
Attorney for Applicants

Registration No. 34,382

FITZPATRICK, CELLA, HARPER & SCINTO  
30 Rockefeller Plaza  
New York, New York 10112-3801  
Facsimile: (212) 218-2200

NY MAIN 279480v1

ATTY DOCKET NO.  
01997.001700APPLICATION NO.  
10/058,024

APPLICANT

FILING DATE  
01/29/02

ANJANA RAO, ET AL.

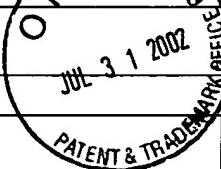
RECEIVED

AUG 01 2002

GROUP  
1645

TECH CENTER 1600/2900

U.S. PATENT DOCUMENTS



*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT

## OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)

		Heidi Okamura, et al., "Concerted Dephosphorylation of the Transcription Factor NFAT1 Induces a Conformational Switch that Regulates Transcriptional Activity", Molecular Cell, Vol. 6, pp. 539-550 (September, 2000).
		Richard A. Houghten, et al., "Generation and use of synthetic peptide combinatorial libraries for basic research and drug discovery", Nature, Vol. 354, pp. 84-86 (November 7, 1991).
		Stefan Feske, et al., "Gene regulation mediated by calcium signals in T lymphocytes", Nature Immunology, Vol. 2, No. 4, pp. 316-324 (April 2001).
		Jörg Heyer, et al., "Inefficient Termination of Antigen Responses in NF-ATp-Deficient Mice", Immunobiol., vol. 198, pp. 162-169 (1997).
		Jan Buer, et al. "Interleukin 10 Secretion and Impaired Effector Function of Major Histocompatibility Complex Class II-restricted T Cells Anergized In Vivo", J. Exp. Med. Volume 187, No. 2, pp. 177-183 (January 19, 1998).
		Rakesh Datta, et al., "Caspase-3-mediated Cleavage of Protein Kinase C θ in Induction of Apoptosis", The Journal of Biological Chemistry Vol. 272, No. 33, pp. 20317-20320 (August 15, 1997).
		Sergei Chuvpilo, et al., "Alternative Polyadenylation Events Contribute to the Induction of NF-ATc in Effector T Cells", Immunity, Vol. 10, pp. 261-269 (February, 1999).
		Wei Fang, et al., "Self-Reactive B Lymphocytes Overexpressing Bcl-x <sub>L</sub> Escape Negative Selection and Are Tolerized by Clonal Anergy and Receptor Editing", Immunity, Vol. 9, pp. 35-45 (July, 1998).
		Dirk Eberhard, et al., "Transcriptional repression by Pax5 (BSAP) through interaction with corepressors of the Groucho family", The EMBO Journal, Vol. 19, No. 10, pp. 2292-2303 (2000).
		Johannes L. Bos, "EMBO Member's Review -- All in the family? New insights and questions regarding interconnectivity of Ras, Rap1 and Ral", The EMBO Journal, Vol. 17, No. 23, pp. 6776-6782 (1998).
		Brian R. Gastman, et al., "Caspase-mediated Degradation of T-Cell Receptor ζ-Chain", Cancer Research 59, pp. 1422-1427, (April 1, 1999).

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 (modified)

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICELIST OF REFERENCES CITED BY APPLICANT(S)  
(Use several sheets if necessary)ATTY DOCKET NO.  
01997.001700APPLICATION NO.  
10/058,024

APPLICANT

ANJANA RAO, ET AL.

JUL 31 2002

FILING DATE  
01/29/02GROUP  
1645

## U.S. PATENT DOCUMENTS

RECEIVED

CLASS

SUBCLASS

FILING DATE  
IF APPROPRIATE

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	AUG 01 2002		
					TECH CENTER 1600/2900		

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT

## OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)

		Stanford L. Reng, et al. "NFATc1 and NFATc2 Together Control Both T and B Cell Activation and Differentiation", Immunity, Vol. 14, No. pp. 13-20 (January 2001).
		Thomas M. Yankee, et al., "CD95 / Fas induces cleavage of the GrpL / Gads adaptor and desensitization of antigen receptor signaling", PNAS, pp. 6789-6793 (June 5, 2001).
		Pierangela Sabbattini, et al., "Binding of Ikaros to the λ5 promoter silences transcription through a mechanism that does not require heterochromatin formation", The EMBO Journal, Vol. 20 No. 11, pp. 2812-2822 (2001).
		Kai Schuh, et al., "Retarded thymic involution and massive germinal center formation in NF-ATp-deficient mice", Eur. J. Immunol. Vol. 28, pp. 2456-2466 (1998).
		David G. Telander, et al., "Evidence for Repression of IL-2 Gene Activation in Anergic T Cells", Journal of Immunology, Vol. 162, pp. 1460-1465 (1999).
		Masashi Toyoda, et al., "Jumonji Is a Nuclear Protein That Participates in the Negative Regulation of Cell Growth", Biochemical and Biophysical Research Communications, Vol. 274, pp. 332-336 (2000).
		James I. Healy, et al. "Different Nuclear Signals Are Activated by the B Cell Receptor during Positive Versus Negative Signaling", Immunity, Vol. 6, pp. 419-428 (April, 1997).
		Martin R. Hodge, et al., "Hyperproliferation and Dysregulation of IL-4 Expression in NF-ATp-Deficient Mice", Immunity, Vol. 4, pp. 397-405 (April, 1996).
		Shintaro Kamizono, et al., "The SOCS Box of SOCS-1 Accelerates Ubiquitin-dependent Proteolysis of TEL-JAK2", The Journal of Biological Chemistry, Vol. 276, pp. 12530-17538 (April 20, 2001).
		Astrid Lanoue, et al., J. Exp. Med., Vol. 185, No. 3, 405-414, (February 3, 1997).
		Lyudmila Lyakh, et al., "Expression of NFAT-Family Proteins in Normal Human T Cells", Molecular and Cellular Biology, p. 2475-2484 (May 1997).
		Xian Chang Li, et al., "The role of T cell apoptosis in transplantation tolerance", Current Opinion in Immunology, Vol. 12, pp. 522-527, (2000).
		Miguel Angel Sanjuán, et al., "Role of Diacylglycerol Kinase α in the Attenuation of Receptor Signaling", The Journal of Cell Biology, Vol. 153, No. 1, pp. 207-219 (April 2, 2001).

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 (modified)

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICELIST OF REFERENCES CITED BY APPLICANT(S)  
(Use several sheets if necessary)ATTY DOCKET NO.  
01997.001700APPLICATION NO.  
10/058,024

APPLICANT

ANJANA RAO, ET AL.

JUL 31 2002

FILING DATE  
01/29/02GROUP  
1645

RECEIVED

PTO &amp; TRADEMARK OFFICE ETC

## U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	AUG 01 2002	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
				TECH CENTER 1600/2900				

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT

## OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)

	<b>Fernando Macián, et al., "Gene expression elicited by NFAT in the presence or absence of cooperative recruitment of Fos and Jun", The EMBO Journal, Vol. 19, No. 17, pp. 4783-4795 (2000).</b>
	<b>Stephen F. Altschul, et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Research, Vol. 25, No. 17, pp. 3389-3401 (1997).</b>
	<b>Sheila Hobbs DeWitt, et al., "Diversomers": An approach to nonpeptide, nonoligomeric chemical diversity", Proc. Natl. Acad. Sci. USA, Vol. 90, pp. 6909-6913 (August 1993).</b>
	<b>Koji Suga, et al., "CD98 induces LFA-1-mediated cell adhesion in lymphoid cells via activation of Rap 1", FEBS letters, Vol. 489, pp. 249-253 (2001).</b>
	<b>Suneet Agarwal and Anjana Rao, et al., "Modulation of Chromatin Structure Regulates Cytokine Gene Expression during T Cell Differentiation", Immunity, Vol. 9, pp. 765-775 (December, 1998).</b>
	<b>Thomas Kamradt, et al., "Tolerance and Autoimmunity", N. Engl. J. Med., Vol. 344, No. 9, pp. 655-664 (March 1, 2001).</b>
	<b>Wei Li, et al., "Blocked Signal Transduction to the ERK and JNK Protein Kinases in Anergic CD4+ T Cells", Science, Vol. 271, pp. 1272-1276 (March 1, 1996).</b>
	<b>William L. Perry, et al., "The itchy locus encodes a novel ubiquitin protein ligase that is disrupted in a 18H mice", Nature Genetics, Vol. 18, pp. 143-146 (February 1998).</b>
	<b>Marc K. Jenkins, et al., "Molecular events in the induction of a nonresponsive state in interleukin 2-producing helper T-lymphocyte clones", Proc. Natl. Acad. Sci. USA, Vol. 84, pp. 5409-5413, Immunology (August 1987).</b>
	<b>Cyrus Chothia, et al., "Canonical Structures for the Hypervariable Regions of Immunoglobulins", J. Mol. Biol., Vol 1996, pp. 901-917 (1987).</b>
	<b>Ronald H. Schwartz, "Models of T Cell Anergy: Is There A Common Molecular Mechanism", The Journal of Experimental Medicine, Vol. 184, pp. 1-8 (July 1996).</b>
	<b>Stephen F. Altschul, et al., "Basic Local Alignment Search Tool", J. Mol. Biol., Vol. 215, pp. 403-410 (1990).</b>
	<b>Steven Xanthoudakis, et al., "An Enhanced Immune Response in Mice Lacking the Transcription Factor NFAT1", Science, Vol. 272, pp. 892-895 (May 10, 1996).</b>

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

ATTY DOCKET NO.  
**01997.001700**APPLICATION NO.  
**10/058,024**

APPLICANT

**ANJANA RAO, ET AL.**FILING DATE  
**01/29/02**GROUP  
**1643**

JUL 31 2002

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	<b>RECEIVED</b>	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
					AUG 01 2002			
					SEARCH CENTER 1600/2900			

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT

## OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)

		Kenneth M. Murphy, et al., "Induction by Antigen of Intrathymic Apoptosis of CD4+CD8+ TCR <sup>+</sup> Thymocytes in Vivo", Science, Vol. 250, pp. 1720-1723 (December 1990).
		Bart Beverly, et al., "Reversal of <i>in vitro</i> T cell clonal anergy by IL-2 stimulation", International Immunology, Vol. 4, No. 6, pp. 661-671 (March 2, 1992).
		Vassiliki A. Boussiotis, et al., "Maintenance of Human T Cell Anergy: Blocking of IL-2 Gene Transcription by Activated Rap1", Science, Vol. 278, pp. 124-128 (October 3, 1997).
		Ada M. Kruisbeek et al., "Mechanisms underlying T-cell tolerance", Current Opinion in Immunology, Vol. 8, pp. 233-244. (1996).
		Anne E. Goldfeld, et al., "Identification of a Novel Cyclosporin-sensitive Element in the Human Tumor Necrosis Factor $\alpha$ Gene Promoter", J. Exp. Med., Volume 178, pp. 1365-1379 (October 1993)
		Patrick E. Fields, et al., "Brocked Ras Activation in Anergic CD4+ T Cells", Science, Vol. 271, pp. 1276-1278 (March 1, 1996).
		Luika A. Timmerman, et al., "Rapid shuttling of NF-AT in discrimination of Ca <sup>2+</sup> signals and immunosuppression", Nature, Vol. pp. 383, (October 31, 1996).
		Kurt Bachmaier, et al., "Negative regulation of lymphocyte activation and autoimmunity by the molecular adaptor Cbl-b", Nature, Vol. 403, pp. 211-216 (January 13, 2000).
		Yungpin J. Chiang, et al., "Cbl-b regulates the CD28 dependence of T-cell activation", Nature, Vol. 403, pp. 216-220 (January 13, 2000).
		Kevin J. Maloy, et al., "Regulatory T cells in the control of immune pathology", Nature Immunology, Vol. 2, No. 9, pp. 816-822 (September 2001).
		P. Garside, et al., "Oral Tolerance", Seminars in Immunology, Vol. 13, pp. 177-185 (2001).
		Chen Wang, et al., "TAK1 is a ubiquitin-dependent kinase of MKK and IKK", Nature, Vol. 412, pp. 346-351 (July 2001).
		Ronald N. Germain, et al., "The Dynamics of T Cell Receptor Signaling: Complex Orchestration and the Key Roles of Tempo and Cooperation", Annu. Rev. Immunol., Vol. 17, pp. 467-522 (1999).

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 ( <i>modified</i> ) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)				ATTY DOCKET NO. <b>01997.001700</b>	APPLICATION NO. <b>10/058,024</b>			
				APPLICANT <b>ANJANA RAO, ET AL.</b>				
				FILING DATE <b>01/29/02</b>				GROUP <b>1645</b>
U.S. PATENT DOCUMENTS								
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE	
							<b>RECEIVED</b>	
							AUG 01 2002	
							TECH CENTER 1600/2900	
FOREIGN PATENT DOCUMENTS								
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT	
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)								
		Anjana Rao, et al., "Transcription Factors of the NFAT Family: Regulation and Function", Annu. Rev. Immunol., Vol. 15, pp. 707-747 (1997).						
		Donna M. Berry, et al., "Caspase-dependent cleavage of the hematopoietic specific adaptor protein Gads alters signalling from the T cell receptor", Oncogene Vol. 20, pp. 1203-1211 (2001).						
		Thomas G. Hofmann, et al., "Caspase-dependent cleavage and inactivation of the Vav1 proto-oncogene product during apoptosis prevents IL-2 transcription", Oncogene Vol. 19, pp. 1153-1163 (2000).						
		Lin Chen, et al., "Structure of the DNA-binding domains from NFAT, Fos and Jun bound specifically to DNA", Nature, Vol. 392, No. 5, pp. 42-48 (March 5, 1998).						
EXAMINER				DATE CONSIDERED				

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Sheet 5 of 5